Exhibit 3

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION	
This document relates to:	MDL No. 2804
The County of Summit, Ohio, et al. v. Purdue Pharma L.P., et al., Case No. 18-op-45090	Hon. Dan Aaron Polster
The County of Cuyahoga, Ohio, et al. v. Purdue Pharma L.P., et al., Case No. 17-op-5004	

CORRECTED AND RESTATED EXPERT REPORT OF KEVIN M. MURPHY, Ph.D.

June 21, 2019

opioids. One would not interpret the regression in 20 to suggest that shipments of prescription opioids cause cancer. A more sensible explanation is that high levels of prescriptions lead to high levels of opioid shipments in areas with high rates of cancer mortality.

Exhibit 20

Changes in Cancer Mortality Are Correlated with But Not Causally Determined by Opioid Shipments

Dependent Variable	Independent Variable	Shipment Coefficient	p value
Change in Cancer Mortality	Cumulative Average Opioid Shipments	2.37	0.09

Sources: ARCOS, NVSS, Census data from Plaintiffs' experts' backup materials.

3. Test 3: Professor Cutler's approach would purport to find illogical cause-and-effect relationships between future shipments of prescription opioids and past mortality

113. As a third example of the danger in interpreting causality when a causal relationship does not exist, I regress the change in opioid-related mortality from 1993-1995 to 2009-2010 on cumulative average shipments between 2011 and 2016. Exhibit 21 shows the coefficient on (future) shipments from this regression. Prescription opioid shipments that have not yet occurred cannot cause increases in mortality, yet the coefficient on 2011-2016 shipments is positive and statistically significant.

Exhibit 21

Changes in Opioid Mortality Are Correlated with But Not Causally Determined by Future Opioid Shipments

Dependent Variable	Independent Variable	Shipment Coefficient	p value
Opioid Mortality	Future Cumulative Average Opioid Shipments	2.14	<0.01

Sources: ARCOS, NVSS, Census data from Plaintiffs' experts' backup materials.

114. Professor Cutler of course does not claim to attribute past harms to future shipments, and he does not attempt to measure the "impact" of future shipments on past harms. It is not correct to interpret the observed relationship between 2011-2016 shipments and changes in 1993-1995 to 2009-2010 opioid mortality as evidence that future shipments cause past mortality. Similarly, it is not correct to interpret, as Professor Cutler does, the observed relationship between 1997-2010 shipments and changes in 1993-1995 to 2009-2010 opioid mortality, as evidence that an exogenous change in shipments leads to opioid-related mortality.

D. The Observed Correlation between Opioid Shipments and Opioid Mortality Does Not Mean That All High Shipment Counties Experienced High Opioid Mortality

1. Professor Gruber's graphical analysis

115. Professor Gruber's Figures I.18, I.19, and I.20 show the average prescription, illicit, and total mortality rates across counties in the top and bottom quartiles of the distribution (weighted by population) of opioid shipments.[100] The conclusion Professor Gruber draws from these figures is that the growth in opioid mortality, from both prescription and illicit opioids, had a strong relationship with per capita shipments of prescription opioids

100 Gruber Report at ¶¶ 84-87.

between 1997 and 2010, "with counties that received more shipments experiencing higher mortality rates."[101] I explained above that an observed correlation between prescription opioid shipments and opioid mortality does not mean that shipments caused mortality. An observed correlation also does not imply that counties that received high opioid shipments always had high levels of opioid-related mortality or that counties that received low opioid shipments always had low levels of opioid-related mortality. On the contrary, many counties in the top quartile of shipments had below-average mortality rates, and many counties in the bottom quartile of shipments had above average mortality rates.

116. Exhibit 22 shows the percentage of counties in the bottom shipments quartile with mortality rates that were higher than the population-weighted mean mortality rate across the 400 counties in Professor Gruber's sample.[102] The exhibit also shows the percentage of the population in the bottom shipments quartile that lives in counties with above-average mortality.

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101 Gruber Report at ¶ 87.

102 I show in Exhibits 22 and 23 the same quartiles as Professor Gruber. Professor Gruber applies weights based on the county population. There are therefore different numbers of counties in each quartile, but each quartile has roughly the same number of people (per the populations of the counties in each quartile). His bottom-shipment quartile is comprised of 68 counties and his top-shipment quartile is comprised of 103 counties. I also apply population weights when determining the mean mortality rate across the 400 counties, which is consistent with how Professor Gruber calculates the mean mortality within the top and bottom quartiles.

Exhibit 22

Many Low-Shipment Counties Have Above-Average Opioid Mortality

Year	National Average Any Opioid Mortality	Share of Counties in **Bottom**-Shipment Quartile with Mortality Rates **Above** the National Average	
		Share of Counties	Share of Population
1999	4.4	15%	50%
2000	4.5	10%	23%
2001	4.7	18%	27%
2002	5.9	9%	22%
2003	6.2	12%	12%
2004	6.3	7%	3%
2005	6.8	15%	9%
2006	7.8	13%	17%
2007	8.2	10%	3%
2008	8.5	10%	3%
2009	8.7	25%	8%
2010	8.8	15%	5%
2011	9.6	19%	6%
2012	9.8	18%	5%
2013	10.3	16%	5%
2014	11.4	16%	5%
2015	13.0	19%	6%
2016	16.7	22%	20%

Source: Backup materials to the expert report of Professor Gruber.

117. The analysis in Exhibit 22 shows that, among counties with the lowest shipments, the share of counties with above-average mortality rates ranges from seven to 25 percent for each year from 1999 through 2016.[103] The percentage of the population living in these counties ranges from three to 50 percent, depending on the year. Thus, a number of counties with relatively few shipments have relatively high opioid mortality rates.

[103] Cuyahoga County is in the bottom second shipment quartile and Summit County is in the third shipment quartile. The opioid mortality rates in Cuyahoga and Summit are sometimes above and sometimes below the national average, depending on the year.

as a general matter to find higher rates of opioid mortality in areas with low levels of opioid consumption. The relationship between consumption and mortality, however, is not informative for understanding or measuring an effect of the alleged conduct at issue in this litigation.

130. As I discussed above in Section VI, under Plaintiffs' experts' methodology, Professor Cutler must ensure that the estimated relationship between opioid shipments and any opioid-related harm is a relationship between the aspect of shipments that the alleged misconduct would affect, and not elements of the demand for opioids (including the demand for opioid misuse and abuse) that are not related to the alleged misconduct. By failing to identify and isolate aspects of opioid consumption affected by the alleged misconduct, Professor Cutler has failed to estimate an impact on mortality that can be used to properly estimate any harms attributable to alleged misconduct.

131. Neither Professor Cutler nor Professor Rosenthal identifies a set of shipments that led to harm in any individual county. Rather, Professor Cutler assumes that any reduction in shipments would reduce "harms." His analysis implies that blocking *all* prescription opioid shipments starting in 1997 would have reduced opioid-related harms by between 49.2 percent (in 2006) and 90.7 percent (in 2016).[111] The elimination of all shipments, however, would mean that patients who need pain medication would not have access to it. Professor Cutler does not factor into his analysis the negative outcomes associated with reducing opioid

[111] *See* Cutler Report Appendix III.I at Table I.4, Column M.

shipments, including the negative outcomes associated with eliminating opioid shipments altogether.[112]

2. Professor Cutler does not control for all of the factors correlated with shipments that influence opioid mortality

132. Professor Cutler includes in his direct model a set of economic and demographic factors "to ensure that estimates of the relationship between shipments and mortality properly control for other factors that might affect opioid mortality."[113] In order for his coefficient on shipments to be used to estimate the share of mortality attributable to the alleged misconduct, his set of control variables would have to capture the aspects of the demand for opioids that are not related to the alleged misconduct. If any factors not captured by Professor Cutler's controls affect mortality and are also correlated with his measure of shipments, Professor Cutler would wrongly attribute the effect of those factors to shipments which, in economic terms, means that his coefficient would be biased.

133. One set of factors that likely affect opioid mortality, and that are unlikely to be completely captured by the economic and demographic factors included in Professor Cutler's

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112 I understand that the expert report of Dr. Gregory Bell discusses in more detail the efficacy of prescription opioids in treating and managing pain. Professor Cutler testified that he is not looking at the benefits to the individual or to society in his analysis, and that he is only looking at harms to the governments of the counties. (Cutler Deposition at 55:15-15-60:23, 220:19-221:10.) He also testified that a benefit of prescription opioids to the county would show up in his model as a reduction in mortality. (Cutler Deposition at 221:18-23.) Professor Cutler, however, does not take into account in his analyses that eliminating prescription opioids as a treatment for pain relief could harm the counties in a way that would not be reflected as reduction in opioid-related mortality.

113 Cutler Report at ¶ 86. I understand that the expert report of Dr. Gregory Bell discusses a number of factors not directly captured by the control variables in Professor Cutler's direct model, that contribute to opioid mortality and to other opioid-related harms, such as addiction, for which Professor Cutler uses mortality as a proxy. Mental health, for example, is sometimes cited as a contributing factor to substance abuse. *See, for example,* "Dual Diagnosis", *National Alliance on Mental Illness*, available at https://www.nami.org/Learn-More/Mental-Health-Conditions/Related-Conditions/Dual-Diagnosis.

model, are the "despair" conditions that I discussed above in Section IV. Imagine a simple model in which the true relationship is:

$$y = \alpha + \beta_1 x + \beta_2 z + \varepsilon \quad [1]$$

where y represents Professor Cutler's measure of mortality, x represents shipments, z represents an omitted variable that measures, for example, the level of despair, and ε represents the error term. If the measure of despair is also correlated with shipments, we can model that similarly:

$$x = \gamma + \delta z + \nu \quad [2]$$

Professor Cutler claims that he is estimating β_1, but is using the following equation:

$$y = \alpha + \tilde{\beta}_1 x + \xi \quad [3]$$

where in this case I use $\tilde{\beta}_1$ to refer to the biased estimator, and ξ represents Professor Cutler's error term which includes variation due to variables that Professor Cutler omits from his regression (in this simple illustration, $\xi = \beta_2 z + \varepsilon$). From [1] and [2] above we can write:

$$y = \alpha + \beta_1 x + \frac{\beta_2}{\delta}(x - \gamma - \nu) + \varepsilon$$

Rearranging the terms yields:

$$y = \left(\alpha - \frac{\beta_2}{\delta}\gamma\right) + (\beta_1 + \frac{\beta_2}{\delta})x + (\varepsilon - \frac{\beta_2}{\delta}\nu) \quad [4]$$

Comparing [3] and [4] we see that Professor Cutler is in fact estimating $\tilde{\beta}_1 = \beta_1 + \frac{\beta_2}{\delta}$, where the bias is indicated by $\frac{\beta_2}{\delta}$. If despair is positively correlated with shipments, and it is also positively correlated with mortality, then both β_2 and δ are positive which means that Professor Cutler is overstating any relationship that may exist between shipments of prescription opioids and mortality.

134. To demonstrate how these conditions would affect Professor Cutler's estimates, I estimated a version of Professor Cutler's direct model in which I included, as an additional control, two measures of non-opioid-related deaths of despair. These are the same two measures that I analyzed in Section VI.C.1 to demonstrate that Professor Cutler's direct model does not establish a causal relationship between prescription opioid shipments and opioid mortality. Here, I use these as proxies for the "despair" conditions that prevailed in many areas of the country and that I discussed in Section IV.

135. Exhibit 26 shows how the inclusion of each these proxies for despair – which I note are not the only addition controls that would be required to reliably estimate a causal relationship between shipments attributable to the alleged misconduct and opioid-related mortality – reduces the magnitude of his shipments coefficient.[114] The exhibit shows the percent reduction in coefficient on shipments relative the coefficient produced by a model similar to Professor Cutler's direct model that does not include the non-opioid "deaths of despair" control. I explained in Section VI.C.1 that the non-opioid deaths of despair measure calculated using Method 1 potentially includes some opioid-related comorbidity, and the measure calculated using Method 2 potentially excludes deaths that would have occurred even in the absence of opioids. Exhibit 26 shows that the inclusion of the Method 1 metric reduces the coefficient by 80 percent and the inclusion of the Method 2 metric reduces the coefficient by 47 percent.

[114] The full set of results from these regressions are in Exhibit C-7 and C-8 of Appendix C. The time period covered by these regressions differs somewhat from Professor Cutler's original regression, so I also include a version of his regression restricted to the same time period as Exhibits C-9 and C-10 of Appendix C.

Exhibit 26

Controlling for Proxies for Despair Conditions Reduces Professor Cutler's Estimates of Impact

Dependent Variable	Additional Control	Shipment Coefficient	p value	Shipment Coefficient from Analogous Regression of Prof. Cutler's Direct Model	Reduction in Impact
		A	B	C	D = (A-C) / C
Change in Opioid Mortality	Non-Opioid "Deaths of Despair" Mortality **Method 1**	0.61	0.13	3.00	-80%
Change in Opioid Mortality	Non-Opioid "Deaths of Despair" Mortality **Method 2**	1.60	<0.01	3.00	-47%

Notes: Deaths of despair include suicide, poisoning by drugs or alcohol, and alcoholic liver disease and cirrhosis, based on the ICD-10 codes used by Case and Deaton (2017). For Method 1, I exclude opioid-related underlying causes of death; for Method 2 I subtract deaths where opioids are underlying or comorbidity causes of death. Professor Cutler's shipment coefficient comes from an analogous regression of Professor Cutler's direct model of opioid drug mortality using the same sample. Because I only have consistent data from CDC Wonder going back to 1999, the dependent variable and economic and demographic control variables are based on changes from 1999-2001, rather than from 1993-1995 as Professor Cutler uses in his direct model. Similarly, the shipments variable is based on cumulative average shipments from 1999-2010 instead of 1997-2010. The full regression results are reported in Appendix C.

Sources: ARCOS, NVSS, Census data from Plaintiffs' experts' backup materials; CDC Wonder.

136. Professor Cutler testified that he controlled for all of the factors that he could think of that would pick up "malaise" (the concept that I refer to as "despair").[115] The analyses in Exhibit 26 show, however, that even simple proxies for despair that were available to Professor Cutler can have a large effect on his results. More generally, the analyses in Exhibit 26 show that it is wrong to interpret Professor Cutler's regression coefficient of 4.39 as measuring the causal impact of shipments on mortality. Rather, the coefficient reflects the effect of factors not included in his model that are correlated with both prescriptions opioid shipments and opioid mortality – his regression analyses establish a correlation only.

115 *See* Cutler Deposition at 305:11-17: "In my analysis I controlled for as many factors as we could possibly get any information on. So it's always possible that one would always want to include additional data if one had it, but we took account of everything that we could think of that would pick up the malaise." *See, also,* Deposition of Jonathan Gruber, April 25, 2019 ("Gruber Deposition"), at 130:2-6: "I did perform a number of analyses and considerations regarding the third possibility that there is an omitted factor causing both [the increase in opioid shipments and the increase in opioid mortality]."

3. Shipments of prescription opioids are driven by prescriptions

137. When discussing the estimates from his direct model, Professor Cutler writes: "The results indicate that, all else equal, each unit increase in shipments between 1997 and 2010 (measured in MME per capita per day) raises the mortality rate by 4.39 deaths per 100,000, an increase of more than 160 percent over the average rate in the base period."[116] This statement implies that opioid shipments functioned as an exogenous variable that, in and of themselves, generated negative outcomes, including opioid abuse and opioid-related mortality. Shipments are not exogenous. The causal chain that leads to shipments includes physicians writing prescriptions, which causes pharmacies to place orders to fill prescriptions, which leads to distributors shipping prescription opioids in response to orders.[117]

138. Exhibit 16 shows the trends in shipments and prescriptions over time for Cuyahoga and Summit counties.[118] The exhibit shows that the trends in prescriptions and

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[116] Cutler Report at ¶ 92. In the estimation of his direct model, Professor Cutler excludes from the data four counties with high levels of shipments. If I estimate his model including the four counties Professor Cutler excluded, the estimated coefficient for the relationship between opioid shipments and mortality is 4.06. By excluding these four counties with large numbers of shipments, Professor increases his coefficient by 8 percent (4.39/4.06 -1 = 0.081). *See* Exhibit C-11 in Appendix C. Professor Cutler testified that he excluded these counties because he suspected that they had high levels of "transshipments" (shipments of prescription opioids to a county that were consumed by people who live in other counties) (*see* Cutler Deposition at 457:19-458:7), but acknowledged that he did not have any direct evidence of transshipments. (Cutler Deposition at 458:15-20: "What we did was we excluded the four counties that were very appreciable outliers in the shipments per capita, which my theory is that there was a good deal of transshipment, but I do not have a direct estimate of that.")

[117] Professor Gruber acknowledges in his report that prescription activity drives shipments. *See*, Gruber Deposition at 441:4-18. *See, also,* Gruber Report at ¶ 74. Professor Cutler testified that prescriptions are correlated with shipments. *See* Cutler Deposition at 643:22-644:3: "The data that we have from Professor Rosenthal's report as well as – I believe other data in the literature, but certainly in Professor Rosenthal's report is that prescriptions track shipments very well over time." *See, also,* Cutler Deposition p. 646:8-9: "Certainly in the aggregate [prescriptions and shipments] are very highly correlated." *See, also,* Cutler Report ¶ 83: "However, the issue affects less than 2.6 percent of the drug shipments in ARCOS, and the correlation between shipments of Schedule II opioids from IQVIA and shipments of all opioids from ARCOS is 0.9973, implying the issue is only minimal importance."

[118] For this analysis, I rely on data from IQVIA used in the analyses presented in the expert report of Dr. Gregory Bell. I understand that these data have limitations. For example, they are based on a sample and therefore do not include the entire universe of prescriptions.

enforcement against 'pill mills' and other forms of diversion of prescription opioids for non-medical use. The FDA pointed to these various factors in their review of whether Purdue's reformulated OxyContin reduced abuse of the drug."[128] All of these changes, Professor Cutler argues, occurred around 2010: "In short, the nature of the opioid crisis changed around 2010. This resulted in a shift in the relationship between shipments of prescription opioids and mortality that has been widely recognized in the economic literature."[129]

150. Professor Cutler assumes that, in years up to 2010, shipments causally affect licit- and illicit-opioid mortality. In his view, in those years, more prescription opioid shipments led to more opioid-related mortality, and fewer prescription opioid shipments led to less mortality. Under Professor Cutler's theory, however, illicit-opioid mortality increased after 2010 because prescription-opioid shipments *decreased*, which led users to switch to illicit opioids. Professor Cutler does not explain this fundamental contradiction embedded in his model, namely that a *decrease* in shipments led to the rise in illicit-opioid mortality after 2010, whereas before 2010 it was an *increase* in shipments that, in his view, led to a rise in illicit-opioid mortality. Professor Cutler cannot have it both ways. If his theory is that a fall in shipments after 2010 led to a rise in illicit-opioid mortality, then by logical consequence, a rise in shipments before 2010 should have led to a decline in illicit-opioid mortality. If, on the other hand, fewer shipments of prescription opioids prior to 2010 would lead to an decrease in illicit-opioid mortality, as Professor Cutler claims to be the case when measures the impact for the 2006 to 2010 period, then fewer shipments should also reduce illicit-opioid mortality after 2010.

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128 Cutler Report at ¶ 52.

129 Cutler Report at ¶ 55.

2. Professor Cutler's indirect model of illicit mortality wrongly attributes any change to the marketplace after 2010 to accumulated shipments of prescription opioids

151. In his indirect model of illicit mortality, Professor Cutler attributes *all* of the changes in the marketplace that led to an increase in illicit mortality after 2010 to opioid shipments.[130] This includes the change in the availability of, prices of, and risks associated with illicit opioids.[131] Professor Cutler acknowledges this in this report. He writes: "The indirect regression attributes the entirety of the unexplained opioid-related mortality to shipments. To the extent that other factors not modelled in the 'baseline' regression contributed to increases in opioid mortality, the indirect approach has the potential to overstate the impact of defendants' actions."[132]

152. Professor Cutler cites several papers in support of his use of an indirect or "residual" model to measure "economic impact."[133] However, for the most part, these papers discuss technological change – a term generally used in economics to refer to an increase in

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130 Professor Cutler testified that, in using his indirect model, he only attributes to the conduct those changes to the marketplace that are not captured by the economic and demographic characteristics that he includes as controls in his model. (Cutler Deposition at 343:18-344:1: "Q. And to be clear, regardless of what the policies were that resulted in increased use of illicit opioids after 2010, your indirect model attributes all of the harm associated with those reductions to the defendants, correct? A. No. It attributes the harm that cannot be explained by the other social and demographics economic changes.") But his economic and demographic factors imply that illicit opioid mortality should have *declined* from 2011 to 2016, which means that Professor Cutler attributes *more* than 100 percent of the increase in illicit mortality to shipments of prescription opioids. In addition, when he estimates his impact percentages, he assumes that some of the illicit mortality in his baseline period was also attributable to shipments of prescription opioids, so the but-for mortality used in his calculations of impact are even lower (which makes the impact higher) than what he shows in his Figure III.5. (*See* Cutler Report Table I.3.)

131 The indirect model that Professor Cutler uses in Approach 2 models all opioid mortality using the years 1993-1995 as the base period. In this model, any changes in the marketplace for illicit or licit opioids from 1996 through 2016 not captured by the economic and demographic factors in the model are attributed to the misconduct. (*See* Cutler Report Figure III.6, ¶¶ 100, 112.)

132 Cutler Report at ¶ 78, footnote 53.

133 Cutler Report at ¶ 80.

output without increased inputs. In one article, economist Robert Solow is discussing an aggregate production function, which is a function of capital and labor units, and a catchall "*t*" to allow for technical change, about which he writes: "It will be seen that I am using the phrase 'technical change' as a short- hand expression for *any kind of shift* in the production function. Thus slowdowns, speed- ups, improvements in the education of the labor force, and all sorts of things will appear as 'technical change.'"[134]

153. Professor Cutler also cites a paper by Joseph Newhouse discussing reasons for increasing medical costs.[135] Newhouse explores several potential explanations for increasing medical costs, then writes: "[b]ecause of the problem in measuring productivity, it is hard to know how much of the increase all the above factors can account for ... I believe the bulk of the residual increase is attributable to technological change, or what might loosely be called the march of science and the increased capabilities of medicine."[136] He then goes on to list several examples of new medical products and procedures as examples of technological change, but adds: "[t]rying to attribute a residual to a specific factor is an inherently frustrating exercise, and the best I can do to support my argument that much of the residual is attributable to the new capabilities of medicine … is to buttress it with data that I believe are consistent with it."[137] Unlike Professor Cutler, Newhouse attempts to do so; Professor Cutler

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134 Solow, Robert M., "Technical Change and the Aggregate Production Function," *The Review of Economics and Statistics vol. 39 No, 3,* August 1957, pp. 312-320, at p. 312.

135 "This method also formed the basis for a widely cited study by Joseph Newhouse arguing that technical change was the primary driver of medical care costs over time." Cutler Report at ¶ 80.

136 Newhouse, Joseph P., "Medical Care costs: How Much Welfare Loss?" *Journal of Economic Perspectives Vol. 6 No. 3,* Summer 1992, pp. 3-21 ("Newhouse (1992)"), at p. 11.

137 Newhouse (1992) at p. 11.

makes no such effort – he simply assumes that the entirety of the residual is attributable to the alleged misconduct.

154. These are not examples of economists conducting analyses of economic impact in the context of estimating a causal relationship between specific factors. Claiming that this literature justifies attributing all of the changes in the marketplace that led to an increase in illicit mortality after 2010 is a mischaracterization of the literature; technological change is inherently difficult to quantify. Plaintiffs, on the other hand, claim to have quantified the alleged misconduct – they should then quantify the relationship between the alleged misconduct and any alleged impact of that conduct, rather than simply assume that all of the changes that they cannot explain are due to the conduct.

155. Professor Cutler disregards the changes in the availability of illicit opioids that contributed to the increase in the use of illicit opioids after 2010. Professor Gruber acknowledges that fentanyl is a "low-cost and high potency alternative to heroin."[138] He points out that fentanyl is more dangerous, that it is more profitable to drug dealers, and that its prevalence increased after 2010.[139] Neither he nor Professor Cutler, however, account for the fact that the changes in the characteristics or prices of illicit opioids before and after 2010 could have led to increased illicit-opioid mortality even in the absence of the alleged misconduct.[140] Indeed, as discussed above, opioid abuse (including prescription opioid abuse)

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138 Gruber Report at ¶ 58.

139 Gruber Report at ¶¶ 55-56.

140 Professor Cutler testified that the introduction of fentanyl was due to the defendants' conduct because the conduct created "thicker markets for illegal opioids." (*See* Cutler Deposition at 365:21-366:14.) Professor Cutler, however, has not shown that the defendants' conduct led to the thickening of markets, or that thick markets led to the introduction of fentanyl. As discussed further below, he has not attempted to measure or characterize the purported thickness of illicit drugs markets and admitted in his deposition that he has no data of the type that would

remained relatively flat or declined over the relevant period, but opioid mortality increased, as would be expected if increases in mortality were caused by the higher prevalence of fentanyl, carfentanil, and other synthetic opioids.

156. Neither Professor Cutler nor Professor Gruber provide statistical evidence that *any* of the changes that led to an increase in mortality related to illicit opioids after 2010 were driven by prescription-opioid shipments, let alone *all* of the changes. Thus, the conclusion I draw is that his indirect model not only has the potential to overstate the impact of the alleged misconduct but also is highly likely to do so.

3. Professor Cutler wrongly implies that all of the changes to regulations around prescription opioids occurred in 2010

157. Professor Cutler's indirect model also relies on the assumption that the relationship between opioid shipments and opioid-related mortality changed radically in or around 2010. He disregards the fact that some of these changes occurred gradually over a multi-year period, rather than all at once in 2010. For example, Professor Cutler cites Prescription Drug Monitoring Programs (PDMPs) as a change that affected the 2011-2016 marketplace.[141] States, however, implemented PDMPs at different points in time over a long period of time, with some states adopting PDMPs in 1990s and others in years after 2010. In addition, the PDMPs were not always immediately accessible to prescribing physicians, pharmacists, and members of law enforcement. Exhibit 29 shows over time the number of states (including the District of Columbia) with a PDMP, and the number with a PDMP that

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be required to form reliable economic opinions about the thickness of illicit drug markets. (*See* Cutler Deposition at 451:2-12; 361:2-17.)

141 Cutler Report Figure III.1. *See, also,* Cutler Report at ¶ 52.

Exhibit 31

Professor Cutler's Indirect Model of Illicit Mortality Produces Inflated Impact Estimates

Comparison to a Single Direct Model with Separate Pre-2010 and Post-2010 Effects

Year	Actual Mortality	Cumulative Average Shipments through 2010	Shipment Coefficient from Regression, 2010	Cumulative Average Shipments, 2011-...	Shipment Coefficient from Regression, 2011-2016	Impact on Mortality	But-For Mortality	Percent Impact on Mortality	Professor Cutler's Indirect Estimate	Percent Difference
	A	*B*	*C*	*D*	*E*	*F = B*C+D*E*	*G = A - F*	*H = F / A*	*I*	*J = I/H - 1*
2011	4.63	1.45	4 34	2.58	-1.91	1.36	3.27	**29.4%**	**64.5%**	**119.3%**
2012	5.54	1.45	4 34	2.57	-1.91	1.39	4.15	**25.1%**	**73.2%**	**191.3%**
2013	7.01	1.45	4 34	2.52	-1.91	1.49	5.52	**21.2%**	**80.0%**	**277.0%**
2014	9.06	1.45	4 34	2.48	-1.91	1.56	7.50	**17.2%**	**86.1%**	**400.0%**
2015	11.78	1.45	4 34	2.44	-1.91	1.64	10.14	**13.9%**	**90.0%**	**546.3%**
2016	16.50	1.45	4 34	2.38	-1.91	1.75	14.75	**10.6%**	**92.9%**	**774.5%**

Source: Backup materials to the expert report of Professor Cutler and CRA analyses.

Exhibit 32

Professor Cutler's Indirect Model of Illicit Mortality Produces Inflated Impact Estimates

Comparison to Mutliple Direct Models

Year	Actual Mortality	Cumulative Average Shipments through 2010	Shipment Coefficient from Regression	Impact on Mortality	But-For Mortality	Percent Impact on Mortality	Professor Cutler's Indirect Estimate	Percent Difference
	A	*B*	*C*	*D = B*C*	*G = A - F*	*H = F / A*	*I*	*J = I/H - 1*
2011	4.63	1.45	0.71	1.03	3.60	**22.3%**	**64.5%**	**189.7%**
2012	5.54	1.45	0.81	1.18	4.36	**21.3%**	**73.2%**	**243.4%**
2013	7.01	1.45	0.87	1.26	5.75	**17.9%**	**80.0%**	**346.3%**
2014	9.06	1.45	1.33	1.93	7.13	**21.3%**	**86.1%**	**304.3%**
2015	11.78	1.45	1.51	2.19	9.60	**18.6%**	**90.0%**	**385.1%**
2016	16.50	1.45	1.55	2.24	14.26	**13.6%**	**92.9%**	**584.1%**

Note: The coefficient in 2016 is not statistically significant indicating that the impact in 2016 is not distinguishable from zero.

Source: Backup materials to the expert report of Professor Cutler and CRA analyses.

D. Professors Cutler and Gruber Have Not Shown That the Defendants' Conduct Prior to 2010 Led to Increased Use of and Mortality from Illicit Opioids after 2010

1. Professor Cutler has not established that all of the changes to the illicit opioid marketplace after 2010 are outcomes of "thicker markets" or that the "thickening" is due to the Defendants' alleged misconduct

161. As motivation for using an indirect approach for estimating the impact of the alleged misconduct on illicit opioid mortality, Professor Cutler asserts that the conduct led to "thicker" markets for illicit opioids: "… the presence and sophistication of drug networks is partially a result of opioid shipments prior to 2010, as they created "thicker markets" for illegal products."[145] He reaffirms this assertion in his deposition testimony:

> *"The decrease in prices associated with heroin to a great extent are because the markets for heroin got to be what economists called thick markets, which is more people…on the supply side, more people on the demand side. The reason they got to be so thick -- the reasons the markets got to be so thick is because there were so many people that had been addicted to opioids, and then when the opioid supply was reduced they went to look for other alternatives, and heroin was a cheaper other alternative. So that led more people into the market. As a result of more people being in the market, there were more sellers, there were more buyers, and in thick markets like that prices tend to fall. I think that the reduction in heroin prices and the increase in heroin use are a result of the factors associated with the opioid – legal opioid epidemic, and they are not some exogenous change that just happened to occur."*[146]

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145 Cutler Report at ¶ 71.

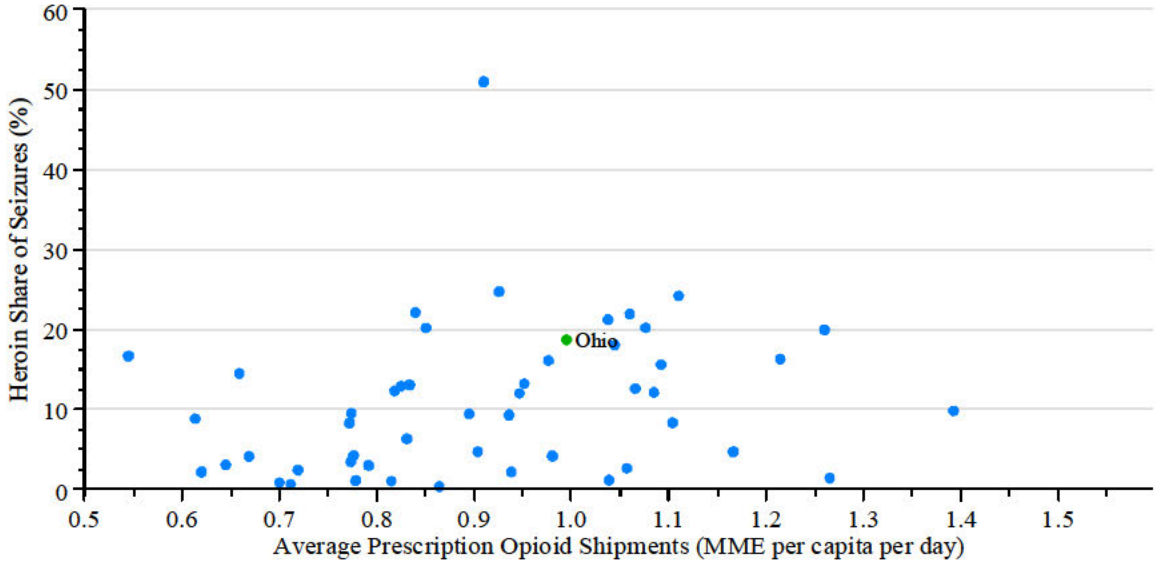
146 Cutler Deposition at 321:16-322:14.

162. Professor Cutler has made no attempt to rigorously define this concept, nor does he quantify it or test this causal link in any way.[147] If it is true, however, that the conduct caused an increase in the supply of illicit opioids, I would expect that he should be able to demonstrate this in a quantifiable way. As Professor Cutler points out, there are no good data on the supply of illicit opioids. There are, however, data on seizures of illicit opioids – the same NFLIS data which Professor Cutler himself uses to estimate the share of drug crimes that are attributable to opioids. If, as Professor Cutler asserts, shipments of prescription opioids in the early 2000s led to an increase in the availability of illicit opioids post-2010, I would expect to see at least a correlation between pre-2010 shipments of prescription opioids and post-2010 seizures of illicit opioids. Using the NFLIS data on the number of times various drugs are identified in drug seizures in each state in each year, I calculate the average share of the seizures recorded in the data that are heroin or fentanyl over the period 2011-2016 for each state. In Exhibits 33 and 34, I plot these against Professor Cutler's measure of cumulative average shipments from 1997 to 2010 for each state. The exhibits show no clear relationship between pre-2010 shipments in a state and post-2010 detection of illicit opioids relative to other drugs seized.

147 Professor Cutler testified that the Alpert and Evans studies cited in his report offered evidence the markets "thickened." (See Cutler Deposition at 324:7-19; *see, also,* Cutler Report at ¶ 61.) The Alpert and Evans studies analyze the effect of the reformulation of OxyContin on heroin use, and conclude that the reformulation caused an increase in the use of heroin. These studies can be interpreted as evidence that OxyContin and heroin are substitutes. The papers do not offer evidence that the market for opioids "thickened," or that the increased availability of prescription opioids led to the increased availability of illicit opioids, including fentanyl. *See* Alpert, Abby, David Powell, and Rosalie Liccardo Pacula, "Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids," *American Economic Journal 10(4),* 2018, pp.1-35, at p. 3; Evans, William N., Ethan M.J. Lieber, and Patrick Power, "How the Reformulation of OxyContin Ignited the Heroin Epidemic," *The Review of Economics and Statistics 101(1),* March 2019, pp.1-15, at p. 1.

Exhibit 33

1997-2010 Prescription Opioid Shipments Are Not Strongly Correlated with 2011-2016 Heroin Seizures

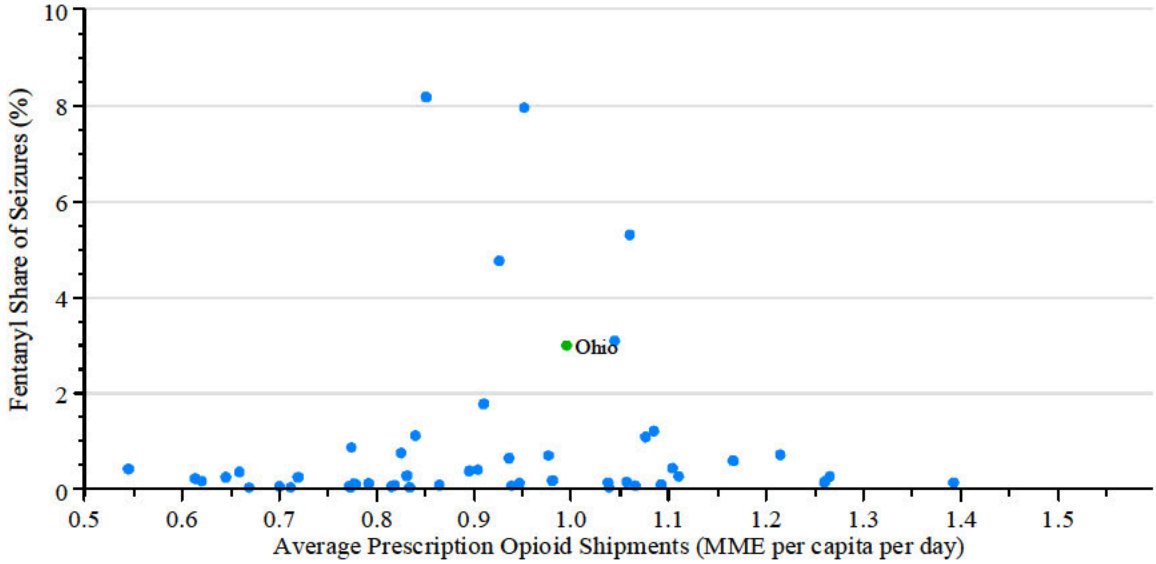


Note: Average prescription opioid shipments is calculated using Professor Cutlers measure of cumulative average shipments.

Source: ARCOS Data from Plaintiffs' experts' backup materials, NFLIS.

Exhibit 34

1997-2010 Prescription Opioid Shipments Are Not Strongly Correlated with 2011-2016 Fentanyl Seizures



Note: Average prescription opioid shipments is calculated using Professor Cutlers measure of cumulative average shipments.

Source: ARCOS Data from Plaintiffs' experts' backup materials, NFLIS.

163. Also notable in these charts is the fact that, while Ohio seems to have a higher than average illicit opioid share of drug seizures, it received a level of shipments of prescription opioids roughly in line with the average across all states. This suggests that factors other than shipments of prescription opioids are driving activity in illicit opioid markets.

164. One assertion that Professor Cutler articulates clearly is his opinion that the reduction in heroin prices is a result of pre-2010 prescription opioid shipments.[148] However, other researchers have found that the declining trend in heroin prices began in the 1990s, and significant price declines had occurred well before 2010. In a 2009 study analyzing the

148 Cutler Deposition at 321:16-18.

increasing supply of heroin from South American origins and the price of heroin in 20 U.S. MSAs over the period 1993-2004, Ciccarone et al. found that as the share of heroin of South American origin increased over the sample period, the price of heroin declined significantly, declining 60 to 89 percent across the cities sampled and 62 percent on average. The authors conclude that, by 2004, these trends had led to "historically low-cost heroin in many US cities."[149]

165. Because this theory of thickening markets is not reliable and is not supported by evidence, the purported causal chain Professor Cutler describes between prescription opioid shipments and illicit opioid mortality is broken.

2. Professors Cutler has not established that prescription opioid use prior to 2010 was a "gateway" to illicit opioid use after 2010

166. In his expert report, Professor Cutler relies on establishing a link between the use of prescription opioids in the pre-2010 period and the use of illicit opioids in the post-2010 period.[150] He cites two epidemiological studies in support of this link. The first is "a survey of heroin patients in drug treatment centers that reported initiating use in the 2000s." According to Professor Cutler, this survey established that 75 percent initiated opioid use with prescription opioids whereas, among respondents that began using opioids in the 1980s, the

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149 Ciccarone, Daniel, George J. Unick, and Allison Kraus, "Impact of South American heroin on the U.S. heroin market 1993-2004," *Int J Drug Policy 20(5)*, September 2009, pp.392-401 ("Ciccarone et al. (2009)").

150 Cutler Report at ¶ 62: "Moreover, a number of epidemiological studies have established that much of the increase in the use of illicit opioids after 2010 was the result of addictions resulting from prior use of prescription opioids." However, Professor Cutler testified at deposition that he is not relying on the gateway theory: "Q. Okay. So I want to talk to you a little bit about the gateway theory. You're familiar with the gateway theory, right? A. Yes, I am familiar with it. Q. And is that something that you separately opine on in this case? A. No, I have not opined upon specifically the gateway theory." (*See* Cutler Deposition at 347:9-17.)

comparable figure was 30 percent.[151] The other is an "analysis of NSDUH survey data," which "established that among respondents that reported using both heroin and prescription opioids (for non-medical use), the share that reported initially using prescription opioids was 83 percent in 2008-10."[152]

167. The studies Professor Cutler cites do not support his conclusion that prescription-opioid use in the pre-2010 period led to heroin and fentanyl use in the post-2010 period. For the "gateway" hypothesis to be true, the probability of using heroin or fentanyl after 2010 must be higher for individuals who used prescription opioids before 2010, holding constant other factors that could lead to the use (or abuse) of both licit and illicit opioids. That is,

$$\text{Prob}(H_t|P_{t-1}, X) > \text{Prob}(H_t|{\sim}P_{t-1}, X) \qquad (1)$$

168. In this equation, H_t is heroin or fentanyl use after 2010, P_{t-1} is prescription opioid use before 2010, ${\sim}P_{t-1}$ is the absence of prescription opioid use before 2010, and X is a set of individual characteristics not caused by prescription-opioid use that could affect heroin or fentanyl use.

169. The studies Professor Cutler cites show that a large number of those who used heroin in the pre-2010 period also misused prescription opioids. That is,

$$\text{Prob}(P_{t-1}|H_{t-1})\ is\ high \qquad (2)$$

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151 Cutler Report at ¶ 62. Professor Cutler cites a 2014 study for these figures. *See*, Cicero, Theodore J., et al., "The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years," *JAMA Psychiatry 70(7)*, 2014, pp. 821-826 ("Cicero et al. (2014)"), at p. 823. In a more recent paper, Cicero and his co-authors note that the use of heroin as an initiating substance had increased since 2005: "the use of heroin as an initiating substance increased from 8.7% in 2005 to 31.5% in 2015." Cicero, Theodore J., Matthew S. Ellis, and Zachary A. Kasper, "Increased use of heroin as an initiating opioid of abuse: Further considerations and policy implications," *Addicted Behaviors 87*, 2018, pp. 267-271 ("Cicero et al. (2018)"), at p.267.

152 Cutler Report at ¶ 62.